The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte MICHAEL SEUL and RICHARD H. EBRIGHT

Appeal No. 2006-0169
Application No. 09/448,420

ON BRIEF[1]

MAILED

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U.S. PATENT AND TRADEMARK OFFICE
BOARD OF PATENT APPEALS
AND INTERFERENCES

Before SCHEINER, MILLS, and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a method of making and screening a library of compounds. The examiner has rejected the claims as anticipated or obvious. We have jurisdiction under 35 U.S.C. § 134. Because the cited references do not teach or suggest all the limitations of the claimed method, we reverse.

Background

"An emerging paradigm for lead discovery in pharmaceutical and related industries such as agricultural biotechnology, is the assembly of novel synthetic compound libraries by new methods of solid state 'combinatorial' synthesis."

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[1] On November 10, 2005, Appellants filed a paper in which they objected to the statement in the Docketing Notice (mailed November 7, 2005) that no oral hearing had been requested. Appellants pointed out that they requested an oral hearing in the Reply Brief. A request for oral hearing, however, must be filed as a separate paper. See 37 CFR § 41.47(b). Therefore, no proper request for oral hearing has been made. The Docketing Notice mailed November 7, 2005, is correct and Appellants' request for a "corrected" Docketing Notice is denied.

Specification, page 1. "One implementation of combinatorial synthesis that is suitable to produce very large chemical libraries relies on solid supports in the form of beaded resins ('beads'). . . . These libraries are screened by performing a wide variety of chemical and biochemical assays to identify individual compounds eliciting a positive response." Page 2.

A problem arises, however, in determining the chemical structure of the compounds that test positive in a given assay. The compounds can be analyzed directly, for example by micro-sequencing or mass spectrometry, but these "methods require the physical isolation of synthesis beads displaying compounds of interest and both require off-line chemical analysis based on substantial amounts of compound." Id.

Another approach is to add coding compounds to each bead that identify each of the chemical synthesis steps that the bead has been subjected to. "Although superior to un-encoded one bead/one compound methods, nevertheless the tagging strategy of [the] prior art still suffers from three limitations. First, individual beads of interest must be physically isolated from the rest; next, molecular tags must be chemically or photochemically cleaved from the bead and cleaved tags must be collected; and finally, chemical analysis (e.g., gas chromatography) must be performed." Pages 3-4.

The specification discloses

> a method to construct several color codes for the purpose of uniquely labeling members of a group of beads . . . to preserve the chemical identity of the beads and thus the identity of bead-coupled chemical compounds. These color codes are based on a set of encoding fluorophores of distinguishable wavelengths, excited-state lifetimes and levels of intensity. . . .
> . . .
> The identity of the compound anchored to any specific bead is determined in-situ by optically probing individual beads to read the color code. . . . This ensures the identification of bead-anchored chemical compounds

without the need for physical separation and without the need for off-line chemical analysis.

Pages 7-8.

Discussion

1. Appellants' motion

On October 31, 2005, Appellants filed a paper styled "Motion for an Interim Order that the Examiner Comply with MPEP Section 1208(A)10, subparts (c) and (e), and Compare 'Feature by Feature' at Least One Claim on Appeal with the Cited Art." In their motion, Appellants alleged that the examiner has not carried out a "feature by feature comparison" of the rejected claims with the prior art, as directed by the MPEP.[2] Appellants requested that the application be returned to the examiner for such an analysis or, alternatively, that this appeal receive an expedited review by the Board.

The motion is granted with respect to the request for expedited review. The appeal has been taken up out of the usual order and processed as expeditiously as possible.

2. Claim construction

Claims 129-151, 154-166, and 168 stand rejected. (Claims 152, 153, and 167 have been withdrawn from consideration and claims 169-174 have been objected to but not rejected.) Claim 129 is the only independent claim on appeal and reads as follows:

129. A method of identifying a compound of interest in a library of compounds, each of said compounds being bound to a solid support and being produced by a unique reaction series composed of N reaction steps, wherein N is an integer of at least 2, and wherein each compound is

[2] Appellants also make other allegations to the effect that the examiner and supervisory patent examiner handling this application have acted in bad faith in an effort to prevent this appeal from being decided. Such allegations have no place in papers filed with this board. We are charged by statute with "review[ing] adverse decisions of examiners upon applications for patents". 35 U.S.C. § 6. We have no supervisory authority with respect to procedural aspects of patent examination. If Appellants wish to complain about the manner in which their application has been examined, those complaints should be addressed to the Director of the appropriate Technology Center.

produced from components which are independently the same or different, the method comprising:

(a) dividing a population of solid support into M batches, wherein M is an integer greater than 1;

(b) reacting each of the M batches of solid support with a component, so that the component forms a bond with the solid support;

(c) adding to one or more batches, prior to (b), concurrently with (b), or subsequently to (b), one or more tag(s), each tag able to be attached to the solid support and able to be identified by optical interrogation, wherein said one or more tag(s) constitutes a code, which code is uniquely associated with a compound and a corresponding reaction sequence and is determined by optical interrogation;

(d) recombining all of said M batches after (b) and (c);

(e) repeating (a) to (d) for N-1 times, or repeating (a) to (d) for N-2 times followed by repeating (a) to (c) once, to produce a library of compounds;

(f) performing an assay capable of indicating that any compound in the library has a property of interest; and

(g) decoding the code composed of one or more tag(s) to identify the compound associated with the code, wherein the decoding step is carried out without isolating the solid support comprising the compound having the property of interest from the other solid supports and without detaching any of the tag(s) from the solid support comprising the compound having the property of interest and wherein said decoding step comprises in-situ optical interrogation of the tag(s).

Thus, claim 129 is directed to a method of combinatorial synthesis in which the components added during synthesis are encoded by tags that are "able to be identified by optical interrogation" (step (c)). The encoding step "preserve[s] the chemical identity of the beads and thus the identity of the bead-coupled chemical compounds." Specification, page 7. The encoding tags are decoded in step (g). Thus, read in light of the specification, the "decoding" means determining the identity of the chemical compound coupled to a bead by analyzing the encoding tag rather than the compound itself. The

decoding is carried out by optical interrogation, without isolating the bead of interest from the other beads, and without detaching any of the tags from the bead of interest.

3. Anticipation by Boyce

The examiner rejected claims 129-151, 160-166, and 168 under 35 U.S.C. § 102(b) as anticipated by Boyce.[3] With respect to the limitations of step (g), the examiner reasoned that "the reference method clearly teaches the positive beads (bright red) with the compound of interest have been identified by visual inspection (in-situ optical interrogation)." Examiner's Answer, page 11.

Appellants argue that, while "Boyce et al. use 'in-situ optical interrogation' to determine which beads turned bright red, determining the positive beads is related to the assay step (f) in both the claim and in Boyce et al., and is not part of 'decoding . . . to identify the compounds' in step (g) or Boyce et al." Appeal Brief, page 8.

We agree with Appellants that Boyce does not teach the limitations recited in step (g) of claim 129 and therefore does not anticipate. Boyce teaches a method of making peptidosteroids using a combinatorial method and screening the bead-bound library "with a dilute solution of substrate tethered to an intensely colored dye. Binding was detected by simple inspection: receptor library beads which bound substrate picked up the color of the dye." Page 7955, right-hand column. Detecting which beads have a property of interest is step (f) in the method defined by claim 129: "performing an assay capable of indicating that any compound in the library has a property of interest."

[3] Boyce et al., "Peptidosteroidal receptors for opioid peptides: Sequence-selective binding using a synthetic receptor library," J. Amer. Chem. Soc., Vol. 116, pp. 7955-7956 (1994).

With regard to step (g) – "decoding the code" – Boyce discloses that they "picked ~ 50 . . . bright red beads and decoded their synthetic histories by gas chromatography." Page 7955, right-hand column. This method of decoding does not meet the limitations of claim 129's step (g). The claim requires that the tags be decoded without isolating the bead of interest from the other beads, while Boyce teaches that they "picked", i.e., isolated, the beads of interest. In addition, the claim requires that the tags be decoded by optical interrogation, while Boyce teaches that they were decoded using gas chromatography. Finally, the claim requires that the tags be decoded without detaching them from the beads, while Boyce teaches decoding by gas chromatography, which reasonably appears to require detaching the tags to be analyzed from the polystyrene beads to which they are attached.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Boyce does not disclose a method meeting all the limitations of claim 129 and therefore does not anticipate the claim.

4. Anticipation by Still

The examiner rejected claims 129-138, 142-146, 151, 155-166, and 168 under 35 U.S.C. § 102(e) as anticipated by Still.[4] The examiner reasoned that Still teaches a method of making and screening a combinatorial library, and that "after the synthesis is completed, the compounds are scre[en]ed for desired property either after detachment of the ligand (compound) from the bead or while still attached (i.e., see column 17, lines 4-6)." Examiner's Answer, page 8. The examiner noted that Still suggests screening

[4] Still et al., U.S. Patent 5,968,736, issued October 19, 1999 (application filed June 7, 1995).

beads using a fluorescence-labelled monoclonal antibody: "The reference teaches that the fluorescent beads with attached compound are identified from the unstained beads, thus, the reference analyzed the fluorescent data of the beads, to identify the compound of interest in the library." Id.

Appellants argue that Still fails to teach at least the limitation of claim 129 that requires the encoding tags to be decoded while attached to the solid support: "There are no statements in Still et al. that the tag/identifier, which is the encoding means of Still et al., does not get removed from the bead for decoding; they consistently state that it in fact does get removed." Appeal Brief, page 16.

We agree with Appellants that Still does not teach every limitation of the method of claim 129. As Appellants have pointed out, Still does not teach a method of analyzing encoding tags without removing them from beads. For example, in column 17, lines 16-18, Still states that "[e]ach selected fluorescent [i.e., antibody-binding] bead is subjected to a means for releasing at least some of the tags from the bead." In the section headed "Tag Analysis", Still states that "[t]ags may be removed from the bead using reductive, oxidative, thermolytic, hydrolytic, or photolytic conditions." Column 31, lines 62-63. In columns 32-33, Still provides guidance on analyzing tags using several chromatographic techniques and mass spectrometry, all of which reasonably appear to require separating the tags from the beads to which they are bound.

More relevant to the instant claims, Still states that "[t]here is also the possibility to use fluorescent tags." Column 33, line 61. Even in this case, however, Still states that the "mixture of tags associated with a particular bead may be detached and subject to an initial separation, where it is desirable to detect each of the tags separately." Column 34, lines 1-3.

The examiner has pointed to no example or direction in Still that would meet the requirement of claim 129 that the encoding tags be decoded while still attached to solid supports. Still does not teach all the limitations of claim 129 and therefore does not anticipate.

5. Anticipation by Dower

The examiner rejected claims 129-138, 142-146, 151, 154, 159-166, and 168 under 35 U.S.C. § 102(b) as anticipated by Dower.[5]

Appellants argue that "Dower et al. do not disclose decoding of tags 'without isolating the solid support of interest from other solid supports' by 'in-situ optical interrogation of the tag,' as in claim 129(g). In Dower et al., beads to be decoded are always isolated." Appeal Brief, page 11.

Although we find Dower to be closer to the claimed method that either Still or Boyce, we agree with Appellants that the reference fails to teach decoding tags without isolating positively-assaying beads. Dower's Example 1 (pages 32-36) is headed "Synthesis of glass beads of 4 fluorescently tagged pentapeptides." In this example, Dower discloses synthesis of four pentapeptides with fluorescent labels that uniquely identify each peptide: Tyr-Pro-Gly-Phe-Leu was labeled with phycoerythrin; Tyr-Gly-Gly-Phe-Leu was labeled with fluorescein and phycoerythrin; Pro-Pro-Gly-Phe-Leu was labeled with Tri-Color; and Pro-Gly-Gly-Phe-Leu was labeled with Tri-Color and fluorescein. The fluorescent tags uniquely identify each of the peptides, so they "encode" the chemical composition of the peptides attached to the beads.

Dower then screened the bead-bound peptides to identify those that were bound by the monoclonal antibody 3E7 (pages 35-36). Dower decoded the tags using flow

[5] Dower et al., WO 93/06121, published April 1, 1993.

cytometry (page 36), which does not reasonably appear to be a technique requiring detaching the tag from the bead, and found that positively-assaying beads "contain both fluorescein and R-phycoerythrin," which reasonably appears to be a result indicating optical interrogation.

In contrast to the method of claim 129, however, Dower isolated antibody-binding beads from beads that did not bind the antibody. See the first full paragraph of page 136:

> A mixture of beads containing [peptides] and their respective tags (see above) are added in phosphate buffered saline (PBS) containing monoclonal antibody 3E7 that has been previously conjugated to colloidal superparamagnetic microbeads. . . . [B]eads which bind the 3E7 antibody are selected using a high strength magnet.

Thus, Dower does not teach a method that includes a "decoding step [that] is carried out without isolating the solid support comprising the compound having the property of interest from the other solid supports," as required by step (g) of claim 129. Dower does not meet all the limitations of claim 129 and therefore does not anticipate.

6. Obviousness

The examiner rejected claims 129-151, 154-166, and 168, under 35 U.S.C. § 103 on the basis that the claimed subject matter would have been obvious in view of Dower and Metzeker.[6] The examiner argued that Metzeker disclosed specific fluorescent dyes that would have been obvious to use in the method taught by Dower. However, the examiner pointed to no disclosure in Metzeker that would have made it obvious to carry out Dower's disclosed method without isolating positively-assaying beads from other beads. Metzeker therefore does not make up for the deficiency of Dower. The rejection under 35 U.S.C. § 103 is reversed.

[6] Metzeker et al., U.S. Patent 5,728,529, issued March 17, 1998 (application filed November 6, 1995).

Summary

The references relied on by the examiner all fail to teach at least one limitation of the instantly claimed method and therefore do not anticipate the claims on appeal. The combination of references relied on by the examiner as a basis for obviousness do not teach or suggest all of the limitations of the claims. The rejections under 35 U.S.C. §§ 102 and 103 are reversed.

REVERSED

Toni R. Scheiner
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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